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Biotechnology Inventions and the Patent Regime

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Abstract: The primary purpose of this paper is to argue that the patent regime for biotechnology may accept patenting fragments of knowledge with the proviso that the formal knowledge and laboratory tools will be made available to everyone who wishes to develop that knowledge towards a marketable product and that the final product manufacturer would be held responsible for sharing the revenues recovered from the market with all the pioneers that contributed to the knowledge development and transfer. This may be, for example, proportional to the costs incurred at successive stages. Such a policy would ensure rapid diffusion of knowledge and technological development while leaving sufficient returns to innovators discoverers at each stage of knowledge accumulation.

Keywords: Biotechnology patents, open source licensing, access to knowledge.

Introduction

The fundamental basis of all developments in biotechnology is the recognition that protein is the key element of all living cells. The earlier chemical-based technologies were directed to understand the chemical structure of proteins, their synthesis, and industrial level production through a fermentation process and other techniques. The classic example is the production of penicillin during the Second World War. The novelty of biotechnology comes from discoveries of the processes by which living cells produce specific proteins to lead cell functions and to create a particular biological activity. In other words, the utilization of chemical processes observed in nature, replaces conventional chemical analysis. These discoveries also make it possible to use bacteria or other genetic manipulations to alter biological activity and in the end clone and produce specific organisms entirely in a laboratory and on an industrial scale.

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The tasks are extensive and each step of the discovery has been very difficult. Part of the reason is the constraint in using two dimensional images obtained through X-ray crystallography and (NMR) scans to identify the three dimensional structure of the protein molecules. Similarly, understanding a vast array of cell functions in the human body or even in plants is a challenging task. As a result, discoveries in biotechnology proceed in a fragmentary way. Only a few cell structures were recorded with difficulty. Examples of this nature are genetically modified cell lines that produce MAbs for diagnosis of diseases and genome data bases that combine sequence data with protein structure. This is typical of scientific progress in all areas of technology and not really specific to biotechnology as such. In general, such fragmentary knowledge must be accumulated and developed toward an ultimate product of use to society. For example, enriched vitamin A rice (popularly called the golden rice) is based on technology that spans 70 patents held by 31 different organizations.

In the past, scientific knowledge was considered a pure public good and made available to anyone who wished to use this to advance it further. Similarly, the universities trained young scientists in the new discoveries and technologies. The private firms then used this pool of talent to implement the technological breakthrough. Similarly, a few years ago, the legalities of obtaining samples of microbes and animals were straight forward. In many instances one could simply arrive at a field site, collect samples, and take them without bothering about legal issues. Samples could be transferred anywhere in the world. It is not possible in today's commercial world. Part of the reason consists in the high costs of R&D and the increasing awareness that knowledge developments at every level have a commercial value.

The issue that had to be addressed is this: what are the most efficient institutional mechanisms to generate R&D, create extensive diffusion of knowledge, preserve the rights of intellectual property, and compensate the pioneers for their discoveries? The most commonly used institutional mechanism is patents. Article 7 of the TRIPS agreement states the objective as,

> "the protection and enforcement of intellectual property rights (with the objective of contributing) to the promotion of technological innovation and to transfer and (disseminate) technology, to the mutual advantage of producers and users of knowledge and in a manner conducive to social and economic welfare, and to balance the rights and obligations".

The basic objective of the rest of the paper is to examine the different institutional mechanisms utilized in practice, to evaluate them with respect to their ability to generate knowledge diffusion and recovery of costs of R&D. The primary contention of this paper is to analyse the efficient patent regime with the proviso that the formal knowledge and laboratory tools will be made available to everyone who wishes to develop that knowledge towards a marketable product, and second that the final product manufacturer shall be held responsible for sharing the revenue recovered from the market with all the pioneers that contributed to the knowledge development and transfer. In the next section, we look into some of these issues.

Biotechnology Patents and Access to Knowledge

Much of the knowledge development, in various scientific activities, was traditionally considered as a public good. This was generally a result of two features. First, most of the scientists, especially those associated with universities had recognition, rather than commercialization, as their primary objective. Second, adequate public funding, in particular for defense related projects, was available. However, over the years, there was no significant involvement of the government in biotechnology R&D primarily because it did not contribute to such defense needs in any major way. Thus, even in the 1960s, secrecy, confined to one research laboratory or a small network of related scientists, was the dominant organizational mechanism. Watson's book, *The Double Helix*, has a graphic description of this approach. The basic reason for this was that a great deal of this fundamental research could not be associated with any product from which the consumers derived value. Secrecy was the only protection for their proprietary knowledge because the patent laws at that time applied the utility doctrine, i.e., usefulness of information to consumers of goods and services as a precondition for the grant of a patent. In the absence of patent protection, secrecy was

the best approach to exclusivity. However, during the early phases of biotechnology research, secrecy was perhaps a result of academic competition instead of any commercial interest.

In the context of several technologies, that are not related to biotechnology, the published formal knowledge was adequate for others to reproduce it and create the materials needed to use it. Fundamentally, there was no specific necessity for the original scientist to participate in the knowledge transfer. Similarly, there was no transfer of any physical materials and laboratory tools along with the knowledge. Biotechnology developments are different in both these respects.

As a result, the developments in biotechnology were proceeding in a fragmented way. Both these features rendered further progress towards a protein structure or a marketable product difficult and inefficient due to secrecy. Removal of findings (e.g., nucleotide sequences) from the public domain restricted development of derivative knowledge necessary to make the genetic information practically usable. Bottazi et al. (2001) noted a further complicating aspect of knowledge generation and transfer. As they pointed out, pharmaceutical inventions are such that imitative product development (reverse engineering, generic drugs) is not very difficult and imitation costs are extremely low in comparison to the inventor's costs. Knowledge erosion is relatively fast since new ideas are generated all the time. These features make advances in knowledge weakly appropriable from the viewpoint of the innovating firm. In particular, any mechanism that rewards only the final product discovery does not compensate the contribution of early innovators which is essential to achieve the latter stage developments. This is the crucial aspect of cost recovery in the context of biotechnology firms.

As with any other innovative endeavour there is no guarantee that every R&D effort will succeed. For instance, biotechnology products may fail at the regulatory stage. These risks, coupled with high costs, necessitate protection at every stage of the value chain. It was the necessary to conceptualize an alternative organizational mechanism that would allow fast and efficient knowledge transfer.

The only well-known organizational mechanism to achieve these ends, viz. achieving efficient knowledge diffusion while providing a

means of recovering costs, was patents. There was some precedence that pointed towards this alternative. First, as far back as 1911, the learned judge Hand upheld a patent on human adrenaline made by using a new process. The patent was not simply for the process but also the purified substance. Second, in 1975 Kohler and Milstein discovered that individual immune system cells, that generate antibodies to a specific antigen, can be fused with immortal cancer cells to create a small factory for producing antibodies. They did not patent it. Hybritech was the first to use monoclonal antibodies in diagnostic kits sold to doctors and hospitals to identify the presence of diseases (e.g. AIDS) or elevated hormonal levels (e.g., pregnancy tests). It received a patent covering the whole family of diagnostic kits. Patents generally provide a 20-year exclusive market protection if the following conditions are satisfied, viz. novelty, non-obviousness and full and complete disclosure so that anyone knowledgeable about the trade can reproduce the production process. In practice, patent claims should also specify their scope. That is, claims should define what the inventor considers to be the technological territory that he claims to be under his control by suing for infringement if necessary.

Note, however, that biotechnology patents cover three types of matter, viz.,

- Products of biotechnology (e.g., seeds, drugs, diagnostic kits);
- Methods and processes of making the biological matter (e.g., fermentation, gene splicing, methods of controlling pests);
- Uses of biological matter (living or non-living) (e.g., antibodies, enzymes, DNA molecules).

The basic problem in granting patents was that much of the biotechnology knowledge was not directed to products of end use. Other objections to patenting genes were:

- They are discoveries (identifying something that already exists) and not inventions;
- Products of nature are not new;
- The basic core of humanity should not be owned by anyone as property.

However, two 1980 decisions of the U.S. Supreme Court changed all that. The Diamond vs. Chakraborty case was about patentability of

a genetically modified bacterium. The court held that such material is patentable because there is novelty. Subsequent, gene or DNA patents have claims that they cover nucleotide sequences that encode genes or fragments of genes. For example, Human Genome Sciences in the U.S. claimed a patent for a gene though its function was not known. It was only asserted that it will be a research reagent or material for diagnostics. Subsequently it was discovered that it was the docking receptor CCR5 used by the HIV virus to infect a cell. Similarly, the U.S. Supreme Court ruled that genetically altered life forms require patenting. A decision by the court allowing an oil company to patent an oil eating microorganism set a precedence and opened up massive possibilities, including that of the exploitation of genetic engineering for commercial purposes. Lakshmikumaran and Pillai (2005) pointed out that the Calcutta high court decision in the Dimminaco A.G. vs. Controller of Patents and designs had a similar basis.

In general, biotechnology patents cover all three types of genetic materials alluded to above. They consist of a combination of definitions of new processes, methods, and compositions. In other words, some genomic discoveries have been granted patents solely on the basis of the new composition or sequences of random pieces of genetic material without knowing its function but only in the hope that it will constitute an important part of a gene. Genetic patents may also be directed to devices for use in testing and diagnostic kits. The pious hope was that patenting knowledge would accelerate its diffusion, help firms obtain finances from venture capital and other sources, and create socially beneficial R&D.

The enlarged scope of biotechnology patents creates a host of new problems. Consider the possibility that a patented biotechnology material requires further improvement and processing before any final product of commercial use emerges. The most obvious example is the Cohen-Boyer patent on rDNA. If another firm wishes to pursue this activity it needs a license from the patent holder. The patent holder may license the use of his patent to others for an appropriate payment. Usually such arrangements have been referred to as material transfer agreements. However, a patent holder may hold rivals hostage if they need licenses for a large number of nucleic acids. For instance, the development of a medicine may depend on genomic technologies,

receptors, assays, and high throughput technologies. This phenomenon is usually designated as patent thickets. It tends to increase the transaction costs of reaching agreements with various owners of the components needed to proceed with product development. The costs may increase prohibitively since each of these patent holders claims a royalty. Property rights generally consist of a right to own and a right to use or rent it to others alongwith a right to modify.

Implicitly such property rights allow the owner to exclude others from the use of such property,

- if he so chooses, and
- if others are not willing to pay the rent specified.

The present day patent regime confers these property rights. However, note that such property rights applied historically to final consumers. The question now is: Should any or all these rights apply to knowledge development as well? Article 27.3 of the TRIPS agreement allows governments of sovereign countries to exclude certain types of inventions from patents if national interests are at stake. That is, one extreme form of reaction is to deny such patent rights altogether. This results in secrecy and hinders knowledge diffusion.

In some cases, like the National Institute of Health in the U.S., the agency stipulates that they will not allow certain types of discoveries of fundamental knowledge to be patented. In the absence of an objective way of classifying different types of knowledge development and specifying entitlements, this remains subjective. The question about financing such R&D is also pertinent. However, this may not be a serious issue so long as adequate public funding is available for all such fundamental research. However, over the years, there has been a reduction in the government involvement in biotechnology R&D primarily because it did not contribute to defense needs in any major way. There is a possibility that R&D financed by such institutions would be inadequate. A further objection may be raised even if adequate finances are provided. In particular, the contribution of any one fundamental R&D to the value addition obtained from a final product of utility may far exceed the cost of generating it. Therefore, any knowledge that contributes to such private value addition in the ultimate analysis should be compensated adequately. Public funding

institutions may not be in a position to ascertain such value additions *apriori* let alone compensate the innovators adequately. In other words, denying patents *per se* also hinders knowledge generation and diffusion.

Rai (2005a) argues that there is a need for improving access by requiring publicly-funded scientists and research institutions to put data and certain types of research into the public domain, or, at a minimum, to license them widely and non-exclusively for a reasonable fees. Non-exclusivity reduces transaction costs and improves the range and quality of resulting products. However, the question of deciding what constitutes reasonable fees cannot be resolved objectively. Further, under the current patent regime, there is no way of compelling private firms to accept exclusivity. Since private R&D constitutes a major portion of biotechnology research this solution is also not adequate.

Some individuals, who patented discoveries, voluntarily agreed to offer non-exclusive access to their knowledge to everyone that may need to use it to move the knowledge forward. The Cohen and Boyer patent for rDNA is one such example. There are two problems with this approach. First, the problem of cost recovery must be resolved. One argument is that in the context of biotechnology mere transfer of formal knowledge will not be sufficient to use it. The scientist, that allows exclusive access to the knowledge he developed, may still charge a consultancy fees for providing the informal knowledge. This may, in itself, be sufficient especially when the use of knowledge spreads widely. Second, there is a possibility that only the manufacturer of a final product sold on the market will usurp all the benefits of the chain of discoveries. Hence, most innovators will be reluctant to use this approach.

Another alternative is to persuade the patent holder to offer his patented knowledge on a collaborative basis or an open source mode. Rai (2005b) makes the case for depending on voluntary action after granting exclusivity. The problem with this argument is as follows. Suppose I am granted a patent with the exclusivity clause in place with a broad scope. Why should I agree to share it free or at a low cost? In particular, a scientist, who is aware that the final product developer is capturing the entire value added, will not accept this arrangement. Rai (2005b) then falls back on the argument that markets in developing

countries add very low value to patents. Hence, she feels that innovators can easily be persuaded to provide patented knowledge to them on a non-exclusive basis. But this creates a variety of new problems if firms in developing countries sell their products in industrial countries. Hence, even this approach is not practical.

If none of the above solutions appear practically feasible the only option is to leave the decision, to enforce exclusivity or leave the knowledge as a public good, to the scientists themselves or the institutions that they belong to. However, the current patent regime has already made them feel that they can derive benefits by exploiting the monopoly power granted by knowledge patents. Consequently, it would be unrealistic to expect them to relent. Rai and Eisenberg (2004) alluded to such attitudes of Wisconsin Alumni Research Foundation (WARF).

It would indeed be paradoxical to grant patent rights, with its implications of property rights, and then expect the patent holders to be persuaded that they should allow non-exclusive use of their patent in the larger interest of social welfare.

Evolving an Institutional Approach

For all practical purposes it is by now acknowledged that discoveries of knowledge need protection by applying the utility doctrine with somewhat greater flexibility (not insisting on utility to a consumer of final products). This appears to be a necessity in the context of biotechnology so that the high costs of R&D can be recovered by private individuals and firms that finance such activities. Exclusivity is granted so that the patent holder may claim royalties from those that use their results of R&D. While patent filing released information in the public domain the exclusivity clause has become a hindrance to knowledge diffusion. Several observers argued a case for narrowing patent rights to restore parity. See, for example, Abrol (2005), Correa (2005), Rangnekar (2006), and Rai (2005b). However, as noted in the previous section, only Rai (2005 a,b) has some analysis of alternatives.

Two situations are conceivable. First, there may be a cumulative chain of 'n' inventions before a final product emerges. Second, a new R&D effort, may be at the downstream level, may require knowledge

embodied in 'n' earlier patented innovations that are not interrelated in the above sense. The requirements of knowledge diffusion in these two cases are somewhat different.

In the first case each stage of invention can be considered as a different marketable product. The patent holder may then be allowed to negotiate a license to a user at the downstream level and extract rents based on the perceptions of the two parties regarding the value added in that particular use. Similarly, he may grant licenses to many firms pursuing different types of applications and developments. However, in line with the conventional patent regime, the patent holder's rights should be deemed to have been exhausted after the first stage license. This reduces the burden of negotiating a license with all the early down stream innovators.

The main advantage of this approach is in allowing faster diffusion of knowledge. It also reduces the burden of transaction costs on the final stage innovator. Clearly, the patent holder at each stage may negotiate the license based on their perception of the value that their knowledge contributes. The only disadvantage is that early stage innovators may not be in a position to assess the ultimate market value of their innovation. Will the patent holder not grant licenses to competitors pursuing the development of the same marketable product? There may be some short-run difficulties. However, long-term reputation will be at stake if such moral hazard persists. Hence, it is unlikely in the long run.

A second approach is more practical and is necessary in the second context. It can also be utilized in the first case. Begin with the observation that the innovator at the final product stage can recover costs when a marketable final product is available. The licensing contract for upstream knowledge is similar to subcontracts for parts and franchise bidding in any other industrial context. Confronted with risks in the ultimate product market the upstream firm may either choose the rents *ex ante* to resolve the risk on wait for the risk to be resolved *ex post* and claim returns accordingly. More often than not, the latter choice is more efficient and it can be implemented if knowledge about the market is not difficult to verify. This suggests the following modification to the patent regime. Suppose that the system

of patenting knowledge is continued with two conditions. one, each of the early stage innovators will be under obligation to provide the knowledge on a non-exclusionary basis. Two, the entire chain of related innovators must be compensated if and when later stage R&D results in a marketable product. This accelerates knowledge diffusion while preserving the appropriability of intermediate discoveries of knowledge. The practical problem of apportioning the eventual benefits among them can be resolved by making payments proportional to the costs incurred at each stage of R&D development. This generally results in recovering more than the costs involved and is closer to the contribution of any one aspect of knowledge to the ultimate value. Hence, the objections raised in the context of public funding of R&D will not arise.

The patent application must normally specify the territory that the applicant considers his own and thus exclude others from it. Hence, the following subtle points can be introduced. First, he may be required to spell out the developments for which the use of knowledge will be allowed on a non-exclusionary basis. Some examples can be offered, namely (a) The knowledge under consideration is not known to result in any marketable product either within the scope of the patent or outside of it. (b) In some cases there may not be any market for early knowledge developments because utility is not obvious. Second, there may be some parts of scientific knowledge that he considers far removed from a final product. In such a case he may be asked to specify the parts of knowledge that he will exclude unless a payment is made.

On the whole, as in the established practice, accepting full property rights for products of utility can be justified. However, they should not apply to at all stages in the context of knowledge development. Otherwise the pious hope that patents will result in extensive knowledge diffusion will not materialize.

Recommendations

However, in general, it must be noted that the new model will be usable only if the patent application contains information about all the prior patented knowledge utilized in the downstream development. It is also necessary for every scientist, at the intermediate stages of development,

to declare the costs of their R&D. From an operational viewpoint there may be a necessity for some institutional mechanism to ensure that payments are properly made and redress grievances if they arise.

An objection to the new scheme may still arise. Note that under the present patent regime a scientist can claim payments as early as possible. What then is the incentive for him to wait until some final product of utility is marketed? Two points may be recorded as possible answers to this question. First, it is well known, from the economic theory of incomplete contracts, that such *ex ante* resolution is inefficient under conditions of risk. Second, under the present patent regime there will be fewer users and/or uses of knowledge that the patent holder developed. This is primarily due to the costs that must be paid before the value is realized and the extensive transaction costs. When the new model is in operation, there will be widespread knowledge diffusion and a better chance of value enhancement. Hence, the losses due to the time lags may be more than compensated. However, it must be acknowledged that this is an empirical matter that any *apriori* judgement about the superiority of one over the other may not be warranted.

Many observers of the current patent regime applied to biotechnology developments acknowledge that exclusivity rights implicitly granted by patents have been a hindrance to knowledge diffusion and enhancement. However, no practical suggestion to overcome this problem has been forthcoming. This paper suggested a practical solution based on the economic theory of incomplete contracts. The new approach requires a slightly more extensive knowledge disclosure from patent applicants. Similarly, there may be an apprehension that the final product manufacturer may not comply with royalty sharing arrangements. In such a case some institutional mechanism to monitor and redress grievances will be necessary. The social cost of such a patent regime may be, however, far less than the welfare gains. It is worthwhile to try it because there will be no problems of patent law in its implementation.

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